DEFINING NITROGEN KINETICS FOR AIR BREAK IN PREBREATH

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ABSTRACT

BACKGROUND: Actual tissue nitrogen (N_2) kinetics are complex; the uptake and elimination is often approximated with a single half-time compartment in statistical descriptions of denitrogenation [prebreathe (PB)] protocols. Air breaks during PB complicate N_2 kinetics. A comparison of symmetrical versus asymmetrical N_2 kinetics was performed using the time to onset of hypobaric decompression sickness (DCS) as a surrogate for actual venous N_2 tension. METHODS: Published results of 12 tests involving 179 hypobaric exposures in altitude chambers after PB, with and without air breaks, provide the complex protocols from which to model N_2 kinetics. DCS survival time for combined control and air breaks were described with an accelerated log logistic model where N_2 uptake and elimination before, during, and after the air break was computed with a simple exponential function or a function that changed half-time depending on ambient N_2 partial pressure. P_1N_2 – P2 = ΔP defined decompression dose for each altitude exposure, where P2 was the test altitude and P_1N_2 was computed N_2 pressure at the beginning of the altitude exposure. RESULTS: The log likelihood (LL) without decompression dose (null model) was -155.6, and improved (best-fit) to -97.2 when dose was defined with a 240 min half-time for both N_2 elimination and uptake during the PB. The description of DCS survival time was less precise with asymmetrical N_2 kinetics, for example, LL was -98.9 with 240 min half-time elimination and 120 min half-time uptake. CONCLUSION: The statistical regression described survival time mechanistically linked to symmetrical N_2 kinetics during PBs that also included air breaks. The results are data-specific, and additional data may change the conclusion. The regression is useful to compute additional PB time to compensate for an air break in PB within the narrow range of tested conditions.

INTRODUCTION

Few data are available to understand the DCS consequences of an air break in an otherwise normal resting 100% O_2 PB, and none are available after PB that includes exercise.

DeHart (1) states, "Air-breathing interruptions of only a few min greatly decrease the efficacy of denitrogenation in the prevention of decompression sickness", but provided no reference.

Berghage (2) says symmetrical N_2 elimination and uptake kinetics should be expected, all else being equal such as no change in cardiac output between elimination and uptake.

But the release of capillary vasoconstriction due to high tissue pO_2 may cause asymmetrical N_2 kinetics.

Estimates for O_2 PB payback time have ranged from one (3) to 35 times (4) the length of the break in PB. Payback time is the numbers of min of additional PB time needed to compensate for an interruption in the original PB time.

METHODS

We used an accelerated log logistic survival model testing for asymmetrical N_2 washout and washin to describe DCS survival times in data from 12 tests from two reports (3,9) where air breaks in the PB were present.

Details about survival models and maximum likelihood optimization are described elsewhere (5-8).

Males ascended to either 3.0 psia in 30 min (n = 91) or to 3.8 psia in 8 min (n = 88) to perform repetitive light exercise plus ambulation for 2 hrs.

The hypothesis is that N_2 washin during an air break is faster than N_2 washout during 100% O_2 PB due to the release of the vasoconstrictive action of high O_2 partial pressure.

Computing Theoretical Tissue N_2 Pressure for Decompression Dose Model

$P_1N_2 = P_0N_2 + (P_aN_{2n} – P_0N_2) * (1 - \exp(-k_n * t_n))$, where P_0N_2 is initial equilibrium tissue N_2 pressure taken as 11.6 psia at sea level, P_aN_{2n} is breathing mixture partial pressure of N_2 over the n^{th} time interval during the PB, t is in min.

for the case of asymmetrical N_2 kinetics, an example is:

$k_n = ((\ln 2 / t_{1/2base}) * (0.078 * P_aN_{2n} + 0.9))$, where k = 0.0028 ($t_{1/2}$ is 240 min) when P_aN_2 = 0 psia and 0.00577 ($t_{1/2}$ is 120 min) when P_aN_2 = 11.6 psia, with $t_{1/2base}$ = 216 min.

Computing P(DCS) for Altitude Exposure P2

$P(DCS)_t = 1 – \exp(- \ln [1 + (P_1N_2 – P2)^{\chi} * (t * \beta)^{\alpha}])$, where t is in hr.

SYSTAT (ver.8) used to compute α, β, and χ coefficients in the accelerated log logistic survival model based on recorded survival times influenced by the PB and exposure conditions of the tests.

RESULTS

A symmetirical 240 min half-time compartment was sufficient (see Table 1) to describe the DCS survival times in 179 exposures that included air break during the PB.

Legend for curves to follow:

Clarke Tests – 30 min ascent to 3.0 psia for 130 min

A = 0 min PB, n = 18 exposures,	100% DCS
B = 60 min PB, 90 min air break, n = 18,	100% DCS
C = 120 min PB, 90 min air break, n = 18,	66% DCS
D = 180 min PB, 90 min air break, n = 18,	33% DCS
E = 120 min PB, n = 19,	26% DCS

Cooke Tests – 8 min ascent to 3.8 psia for 120 min

F = 180 min PB, n = 17 exposures,	0% DCS
G = 60 min PB, 5 min break, 125 min PB, n = 10	20% DCS
H = 120 min PB, 5 min break, 65 min PB, n = 11	9% DCS
I = 180 min PB, 5 min break, 5 min PB, n = 10	10% DCS
J = 60 min PB, 10 min break, 130 min PB, n = 13	7.7% DCS
K = 120 min PB, 10 min break, 70 min PB, n = 12	8.3% DCS
L = 180 min PB, 10 min break, 10 min PB, n = 15	6.7% DCS

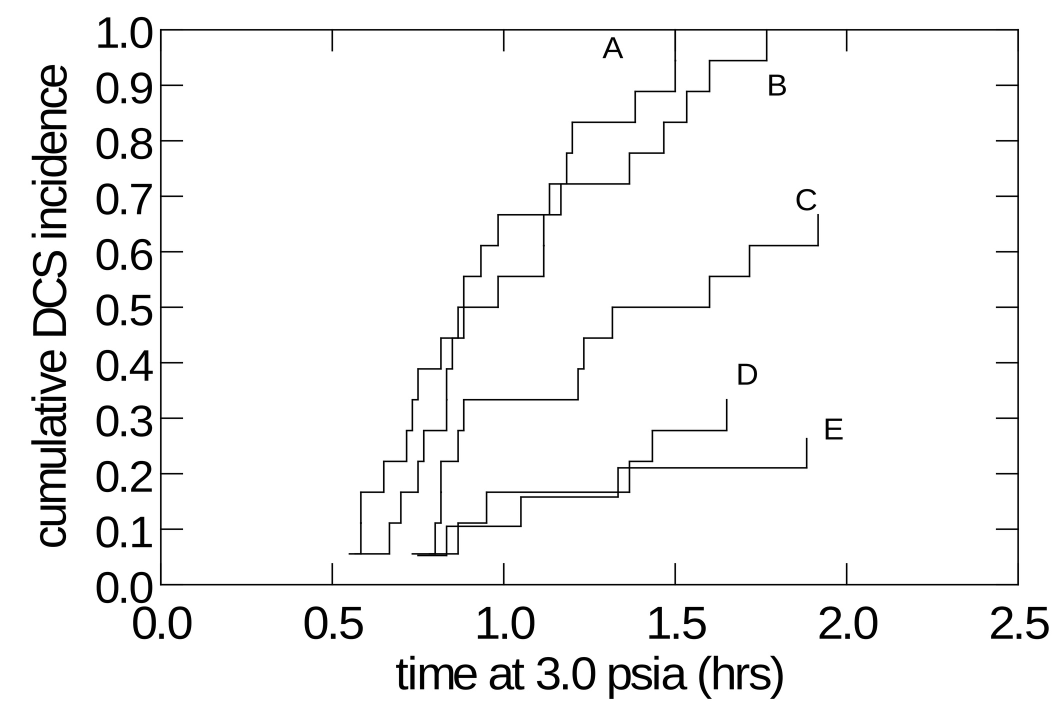

Fig.1 shows the pattern of cumulative DCS incidence for the three curves for air breaks (B,C,D) compared to two curves without air break, but different duration of initial PB (A,B). There is an effect of air break on the pattern of DCS failure times when referenced to the controls.

TABLE 1. MODEL RESULTS TO DESCRIBE DCS SURVIVAL TIMES

model	LL, p – value*
log logistic survival (null model)	-155.59
accelerated log logistic survival	
$(P_1N_2 – P2)^{\chi}$	
P_IN_2 $f(360\ t_{1/2})$	-98.00, p < 0.01
P_IN_2 $f(360\ t_{1/2} + 36\ t_{1/2})$	-108.96, p < 0.01
P_IN_2 $f(240\ t_{1/2})$	**-97.23, p < 0.01**
P_IN_2 $f(240\ t_{1/2} + 120\ t_{1/2})$	-98.91, p < 0.01
P_IN_2 $f(180\ t_{1/2})$	-97.54, p < 0.01
$[(P_1N_2 / P2) – 0.79]^{\chi}$	
P_IN_2 $f(240\ t_{1/2})$	-99.21, p < 0.01
P_IN_2 $f(180\ t_{1/2})$	-98.84, p < 0.01

*LL is computed log likelihood from survival analysis regression, p – value is from Likelihood Ratio Test where p < 0.05 indicates improvement in the model with one additional degree of freedom (fitted parameter).

TABLE 2. REGRESSION RESULTS, N = 179 EXPOSURES

model	log likelihood	parameters	standard error	correlation matrix
Log logistic null model	-155.59	α = 1.92 β = 0.39	0.208 0.036	$\alpha\beta$ = 0.52
Best log logistic accelerated model	-97.23 p < 0.01	α = 3.08 β = 0.027 χ = 5.60	0.314 0.010 0.638	$\alpha\beta$ = 0.47 $\alpha\chi$ = 0.48 $\beta\chi$ = -0.53

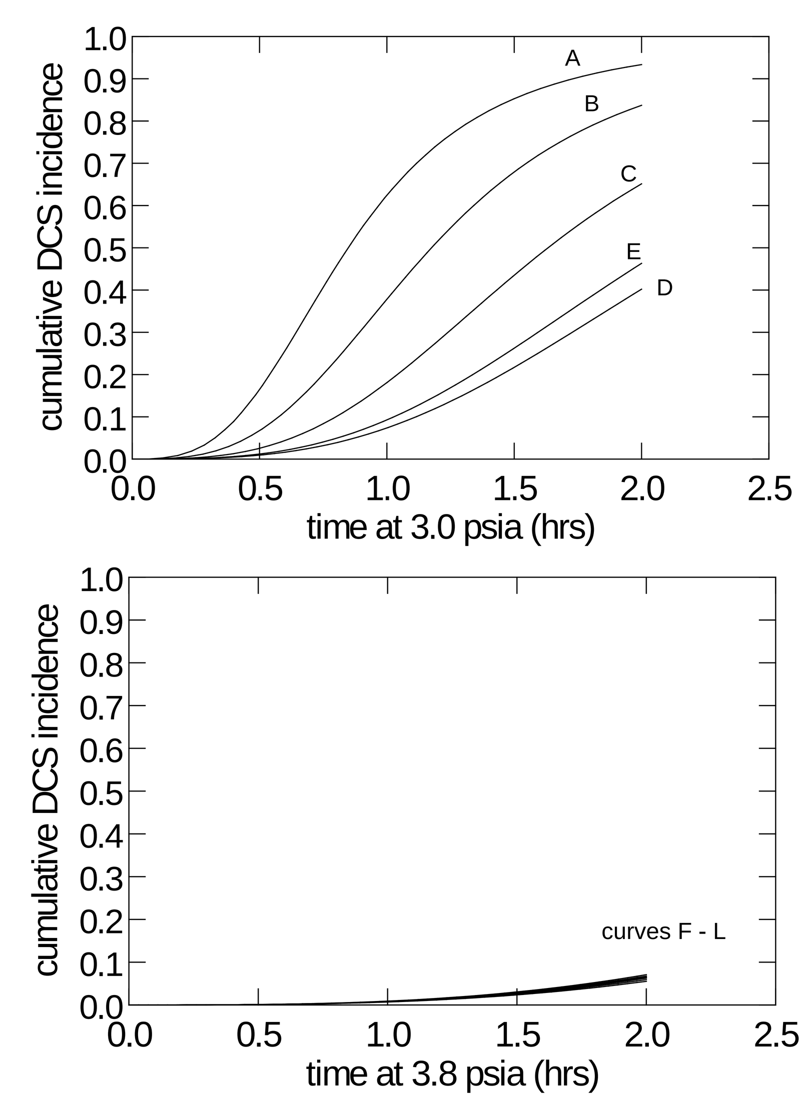

Fig. 2 shows results from predictive survival model from 179 exposures: $P(DCS)_t = 1 – \exp(- \ln [1 + (P_1N_2 – P2)^{5.6} * (t * 0.027)^{3.08}])$. Mean P_1N_2 for curve A = 10.93 psia, 9.63 for B, 8.53 for C, 7.61 for D, 7.82 for E, 6.92 for F, 6.85 for G, 6.87 for H, 6.89 for I, 6.78 for J, 6.82 for K, and 6.86 for L, and P2 is either 3.0 or 3.8 psia.

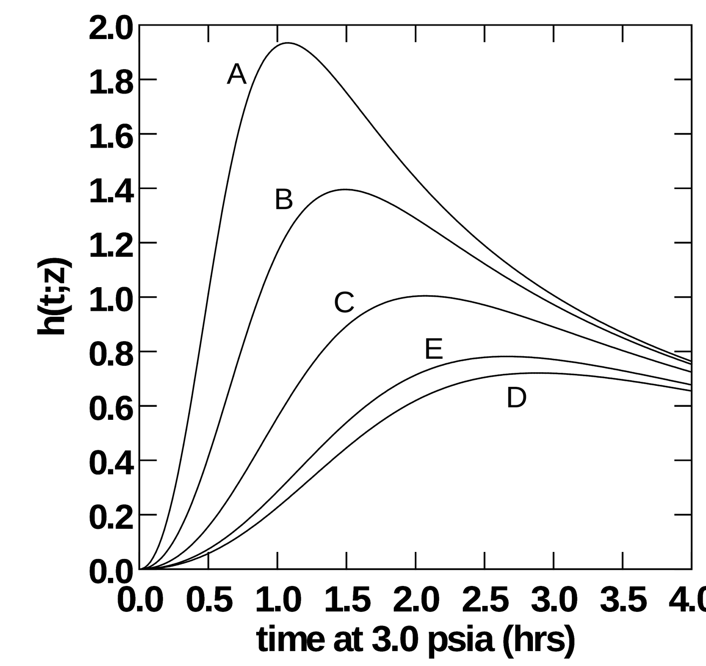

Fig. 3 shows the hazard curves from the accelerated log logistic survival model for the Clarke (8) data. The hazard function defines the instantaneous failure rate at a specific time, given that the subject survived to at least that specified time without DCS. It is expressed as a rate (hr^{-1}). The hazard function for curve A is: $h(t;z) = 3.08 * (10.93 – 3.0)^{5.6} * t^{(3.08-1)} * 0.027^{3.08} / [1 + (10.93 – 3.0)^{5.6} * (t * 0.027)^{3.08}]$.

CONCLUSIONS / DISCUSSION

A simple symmetrical half-time compartment is all that was statistically justified to describe survival time to DCS in these few data. The survival model with ΔP as decompression dose is very simple, but utilitarian.

Computing PB payback time after an air break is a practical application of the survival model. A PB is complex, it can be short or long, and the location of an air break can be early or late into the PB, and the duration of the air break can be short or long. So a quantitative approach to compute PB payback is useful.

For example, an operational task requires that the incidence of DCS not exceed 5% at the end of a two hr exposure to 3.5 psia in someone that performs ambulatory activity. A 200 min PB with a five min ascent is sufficient to restrict the P(DCS) $\leq$ 0.05.

A 30 min air break 60 min into this PB requires five min of additional PB before ascent.

A 30 min air break 180 min into this PB requires 19 min of additional PB before ascent.

The approach to compute O_2 payback time is not appropriate outside the range of tested conditions.

The results are data-specific, and additional data over a wider range of condition will likely change the current conclusions.

The regression model has not been prospectively validated, so the conclusions about payback time are hypotheses rather than recommendations.

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